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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/695,451	10/24/2000	Brenda F. Baker	ISPH-0518	2604

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EXAMINER

SCHULTZ, JAMES

ART UNIT PAPER NUMBER

1635

DATE MAILED: 04/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/695,451

Applicant(s)

BAKER ET AL.

Examiner

J. Douglas Schultz

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 November 2003 and 10 February 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,2 and 4-15 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,2 and 4-15 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Status of Application/Amendment/Claims

1. Applicant's response filed February 10, 2004 has been considered. Rejections and/or objections not reiterated from the previous office action mailed July 16, 2003 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.
2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
3. The examiner acknowledges the telephonic interview that took place on February 9, 2004, in which it was agreed that the previously issued Notice of Non-responsive Amendment would be vacated and the 2 claimed regions of SEQ ID NO: 3 would be searched. Examination on the merits of the claim set first submitted on November 4, 2003 is set forth below.

Response to Claim Rejections - 35 USC § 35 U.S.C. § 103(a)

4. Claims 1, 2, and 5-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ojwang et al. (Biochemistry 1997, 36:6033-6045), in view of Taylor et al. (Drug Disc. Today, 1999, 4(12)562-567) and Baracchini et al. (U.S. Patent Number 5,801,154), for the same reasons of record as cited in the Office action mailed July 16, 2003.

Applicants traverse this rejection by arguing that while Ojwang et al. teaches targeting the coding region, Ojwang does not teach that this targeting was successful. Applicants thus argue that Ojwang teaches away from targeting the region of the coding region claimed now by applicants. This is not considered convincing, because Ojwang nevertheless teaches the

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successful antisense-mediated inhibition of TNFR1 using modified oligos. While it is true that one of the several oligos of Ojwang targeted the translation initiation site, which is considered by applicants to include the coding region as instantly claimed, and that this oligo did not inhibit the translation of applicants instant transcript, this is not considered to teach away from targeting the instant coding region because Ojwang et al. teaches several other modified oligos that do inhibit the translation of TNFR1. Furthermore, while not every oligo is expected to cause inhibition, applicants claimed region for targeting is a particularly broad region of the target, constituting the largest region of the cDNA. This stands in opposition to the target region of the one failed oligo of Ojwang, who targets the translation initiation codon, which is a very small region of the overall target. The fact that Ojwang alone teaches several other oligos capable of causing inhibition indicates that the likelihood of finding at least one that inhibits by targeting the broad coding region are excellent. Furthermore, Baracchini et al. and Taylor et al. teach that it is routine to screen for oligos that are capable of target inhibition while Baracchini provides detailed protocols for such screening procedures. Because Baracchini teaches that the coding region is a preferred target region, and since both Taylor and Baracchini indicates that one of ordinary skill would reasonably expect success in finding oligos capable of achieving inhibition, one of ordinary skill would expect to find at least one if not many more oligos capable of targeting the broad coding region recited by applicants to achieve target inhibition.

Regarding Applicants arguments that the combination of references do not teach targeting regions other than applicants' instantly defined region, it is pointed out that applicants region is large enough to encompass the majority of the entire coding region of the molecule, and is thus considered to consist essentially of the entire coding region. Since Ojwang indicates that

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regions other than the coding region have been shown to have inhibitory efficacy, and because Baracchini specifically state that the coding region is a preferred targeting region, and finally because applicants claimed region of SEQ ID NO: 1 covers much if not most of the coding region, antisense molecules targeted to the region of SEQ ID NO: 1 defined by applicants are considered obvious in view of the cited art.

Applicants' further argue that the secondary references fail to make up for the alleged deficiencies of Ojwang. However, since Ojwang is not considered deficient for the reasons given above, applicants arguments regarding the secondary references are not convincing. Applicants argue that when viewed alone, neither of Taylor et al. or Baracchini et al. teach or suggest antisense compounds targeted to the specific regions of the TNFR1 transcript of SEQ ID NO: 1 as presently claimed. This argument is not adopted. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). It is acknowledged that the references when viewed individually do not teach the presently claimed invention; however, the test for obviousness is what the *combined* teaching of the prior art would have suggested to those of ordinary skill in the art. As indicated above, one of ordinary skill in the art would have been motivated to make antisense oligonucleotides, because the prior art teaches antisense inhibitors of TNFR1 (i.e. Ojwang), and further teaches targeting within the same region targeted by applicants (i.e. Baracchini et al.). Moreover, because Baracchini et al. teach that synthesizing and using antisense oligos to inhibit transcripts of known sequence is routine to one of ordinary skill in the art, this combination also provides a reasonable

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expectation of success which render the invention of the claims above obvious under 35 U.S.C. § 103(a).

Claim Rejections - 35 USC § 102/103

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 and 103 that form the basis for the rejections under these sections made in this Office action:

A person shall be entitled to a patent unless –

102(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

102 (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

103(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1, 2, 12 and 14 are rejected under 35 U.S.C. 102(b) and 103(a) as being anticipated and/or obvious by Draper et al. (U. S. Patent Number 5,514,577).

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The claims of the above invention are drawn to antisense compounds 8 to 30 nucleotides in length that specifically hybridizes with and inhibits the expression of TNFR1 of SEQ ID NO: 1, and which optionally are in composition with pharmaceutically acceptable diluents or are antisense compounds.

SEQ ID NO: 37 possesses 100% identity with residues 1257-1266 of the instant application, and would thus specifically hybridize with TNFR1 of SEQ ID NO: 1. Although these references do not specifically teach the function of inhibiting applicants' instant SEQ ID NO: 1 as claimed in the present application, each of the above-listed compounds meet all the structural limitations as set forth in the instant claims. Because the sequences are substantially identical to applicant's claimed compounds, in the absence of evidence to the contrary said compounds are thus considered to possess the functional limitations of specifically hybridizing with and inhibiting the expression of applicants' instant SEQ ID NO: 1. Support for this conclusion is drawn from MPEP 2112:

Where applicant claims a composition in terms of a function, property or characteristic and the composition of the prior art is the same as that of the claim **but the function is not explicitly disclosed by the reference, the examiner may make a rejection under both 35 U.S.C. 102 and 103, expressed as a 102/103 rejection.** "There is nothing inconsistent in concurrent rejections for obviousness under 35 U.S.C. 103 and for anticipation under 35 U.S.C. 102." *In re Best*, 562 F.2d 1252, 1255 n.4, 195 USPQ 430, 433 n.4 (CCPA 1977). This same rationale should also apply to product, apparatus, and process claims claimed in terms of function, property or characteristic. Therefore, a 35 U.S.C. 102/103 rejection is appropriate for these types of claims as well as for composition claims. *Emphasis supplied.*

In rejecting the claims of the above under 35 U.S.C. 102 and 103, a prima facie case has been established by the examiner whereby the burden of proof in showing that the claimed compounds are not anticipated by the compound(s) of the prior art as stated lies with the applicant, as per MPEP 2112.01:

Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or

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obviousness has been established. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not. *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the prima facie case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. *In re Best*, 562 F.2d at 1255, 195 USPQ at 433.

Thus, in the absence of evidence to the contrary, the antisense compounds of the above listed claims of the instant application are considered anticipated and/or obvious as outlined above.

6. Claims 1, 2, 12 and 14 are rejected under 35 U.S.C. 102(e) and 103(a) as being anticipated and/or obvious by Le et al. (U. S. Patent Number 5,656,272).

The claims of the above invention are drawn to that as discussed above.

SEQ ID NO: 15 possesses 100% identity with residues 835-852 of the instant application, and would thus specifically hybridize with TNFR1 of SEQ ID NO: 1. Although these references do not specifically teach the function of inhibiting applicants' instant SEQ ID NO: 1 as claimed in the present application, each of the above-listed compounds meet all the structural limitations as set forth in the instant claims, for the reasons set forth above.

Double Patenting

7. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 2, and 5-16 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-11 of U.S. Patent No. 6,007,995. This rejection is repeated for the same reasons of record as set forth in the Office action mailed January 3, 2003. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1-11 of U.S. Patent No. 6,007,995 are drawn to specific sequences which anticipate the above-listed claims of the instant application. Applicants have not provided arguments to rebut to this rejection.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

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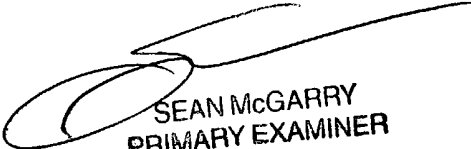
Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. Douglas Schultz whose telephone number is 571-272-0763.

The examiner can normally be reached on 8:00-4:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on 571-272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

James Douglas Schultz, PhD


SEAN MCGARRY
PRIMARY EXAMINER
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